

In the claims:

Please amend the claims as follows:

1-18. (cancelled).

19. (withdrawn). A chimeric receptor containing two or more independent polypeptide chains, each of said chains comprising in N- to C-terminus sequence:

- (1) an extracellular ligand association domain;
- (2) a spacer domain;
- (3) a transmembrane domain; and
- (4) one or more intracellular domains; provided that at least two of said domains in one chain are not naturally fused to each other, and wherein the spacer and/or transmembrane domains are selected to remain unassociated except in the presence of bound ligand.

20. (withdrawn). A chimeric receptor according to Claim 19 wherein each extracellular ligand association domain is an antibody variable region (V_H or V_L) domain, a T-cell receptor variable region domain ($TCR\alpha$, $TCR\beta$, $TCR\gamma$, $TCR\delta$), $CD8\alpha$, $CD8\beta$, $CD11a$, $CD11b$, $CD11c$, $CD18$, $CD29$, $CD49a$, $CD49b$, $CD49c$, $CD49d$, $CD49e$, $CD49f$, $CD61$, $CD41$ or $CD51$ chain or a fragment thereof.

21. (withdrawn). A chimeric receptor according to Claim 20 wherein each association domain is structurally different to each other.

22. (withdrawn). A chimeric receptor according to Claim 19 wherein the ligand association domains of the chimeric receptor are a V_H domain paired with a V_L domain, two or more $TCR\alpha$, $TCR\beta$, $TCF\gamma$, and/or $TCR\delta$ domains, a $CD8\alpha$ or β homo- or heterodimer, $CD18$ paired with one or more of $CD11a$, b , or c , $CD29$ paired with one or more of $CD49a$, b , c , d , e , or f , and $CD61$ paired with $CD41c$ and/or $CD51$.

23. (withdrawn). A chimeric receptor according to Claim 19 wherein each intracellular domain is a naturally occurring polypeptide signaling sequence.
24. (withdrawn). A chimeric receptor according to Claim 23 wherein each signaling sequence is all or part of the zeta, eta or epsilon chain derived from the T-cell receptor; CD28; CD4; CD8; the γ chain of an Fc receptor; a signaling component from a cytokine receptor, a colony stimulating factor receptor, a tyrosine kinase and binding domains thereof; or an adhesion molecule.
25. (withdrawn). A chimeric receptor according to Claim 19 wherein the transmembrane domain is an oligo- or polypeptide derived from all or part of the alpha, beta or zeta chain of the T-cell receptor, CD28, CD8, CD4, CD3 ϵ , CD45 and members of the tetraspan family, a cytokine receptor, or a colony stimulating factor receptor.
26. (withdrawn). A chimeric receptor according to Claim 19 wherein each spacer domain is a polypeptide comprising 20 to 100 amino acids.
27. (withdrawn). A chimeric receptor according to Claim 19 wherein each independent polypeptide chain has a secretion signal sequence attached to the N-terminus of the association domain of each chain.
28. (withdrawn). A chimeric receptor according to Claim 19 wherein the chimeric receptor has two independent polypeptide chains.
29. (withdrawn). A chimeric receptor according to Claim 28 wherein one polypeptide chain has a ligand association domain which is a V_H domain or a fragment thereof, and the other has a ligand association domain which is a V_L domain or a fragment thereof.
30. (withdrawn). A chimeric receptor of Claim 19, wherein the spacer domain is modified to remain unassociated except in the presence of bound ligand.

31. (withdrawn). A chimeric receptor of Claim 19, wherein the transmembrane domain is modified to remain unassociated except in the presence of bound ligand.
32. (withdrawn). A chimeric receptor of Claim 19, wherein the spacer domain is a CD8 domain.
33. (withdrawn). A chimeric receptor of Claim 32, wherein the CD8 spacer domain is a modified CD8 spacer domain.

34. (currently amended). A nucleic acid sequence encoding a chimeric receptor of ~~Claim 19 or an independent polypeptide chain thereof~~, wherein the chimeric receptor contains two independent polypeptide chains, a first polypeptide chain and a second polypeptide chain, wherein the first polypeptide chain comprises in N- to C-terminus sequence:

- (1) an extracellular ligand association domain of an antibody heavy chain variable region;
- (2) a spacer domain of any polypeptide comprising 20 to 100 amino acid residues;
- (3) a transmembrane domain of any oligonucleotide or polypeptide derived from all or part of a human CD4 transmembrane domain; and
an intracellular domain, wherein the intracellular domain is a signaling domain comprised of any naturally occurring polypeptide signaling sequence that is all or part of the human CD4 intracellular signaling domain;

and wherein the second polypeptide chain comprises in N- to C-terminus sequence:

- (4) an extracellular ligand association domain of an antibody light chain variable region;
- (5) a spacer domain of any polypeptide comprising 20 to 100 amino acid residues;

(6) a transmembrane domain of any oligonucleotide or polypeptide derived from all or part of a human CD4 transmembrane domain; and
an intracellular domain, wherein the intracellular domain is a signaling domain comprised of any naturally occurring polypeptide signaling sequence that is all or part of the human T cell receptor zeta chain;

wherein the spacer and/or transmembrane domains of the first and second polypeptide chains are selected to remain unassociated except in the presence of bound ligand.

35 (previously presented). A nucleic acid sequence according to Claim 34 in association with a carrier.

36. (previously presented). A nucleic acid sequence according to Claim 35 wherein the carrier is a viral vector, a liposomal vector, a cationic lipid or an antibody.

37. (previously presented). A nucleic acid sequence according to Claim 35 wherein the carrier is a targeted carrier.

38. (previously presented). A nucleic acid sequence according to Claim 34 wherein the nucleic acid sequence is on a plasmid.

39. (currently amended). A nucleic acid sequence according to Claim 34 wherein the nucleic acid sequence is on a plasmid, wherein the plasmid is ~~Plasmid~~ pHMF374 of Figure 3.

40. (withdrawn). An effector cell containing a nucleic acid sequence or a plasmid according to Claim 34.

41. (withdrawn). An effector cell expressing a chimeric receptor of Claim 19.

In the specification:

Please amend the specification by adding the following passage at page 3, after line 14 and before line 15:

BRIEF DESCRIPTION OF THE DRAWINGS

Figure 1 shows construct cassettes cloned into pBluescript KS+®.

Figure 2 shows oligonucleotide sequences for chimeric receptor construction.

Oligonucleotides are presented in 5' and 3' orientation and are as follows: S4501 (SEQ ID NO: 1); S4502 (SEQ ID NO: 2); S4503 (SEQ ID NO: 3); S4504 (SEQ ID NO: 4); S4881 (SEQ ID NO: 5); S4882 (SEQ ID NO: 6); S4883 (SEQ ID NO: 7); S4884 (SEQ ID NO: 8); S4885 (SEQ ID NO: 9); S4886 (SEQ ID NO: 10); S4499 (SEQ ID NO: 11); S4500 (SEQ ID NO: 12); S4700 (SEQ ID NO: 13); and S4701 (SEQ ID NO: 14).

Figure 3 shows double gene expression plasmids for separate chain chimeric receptors, including: pHMF367; pHMF370; and pHMF374.

Figure 4 shows a histogram revealing stimulation of separate chain receptors with HL60 target cells.

Figure 5 shows a histogram revealing stimulation of separate chain receptors with NSO cells transfected with a control plasmid or a CD33-expressing plasmid.

Please replace the paragraph on page 12, lines 24-28 with the following paragraph:

Each component of the chimeric receptor was either PCR cloned or PCR assembled by standard techniques (PCR Protocols, Innis *et al* (1990) Academic Press Inc.) and sub-cloned in a cassette format into pBluecript KS+® (Stratagene), see Figure 1. Oligonucleotides (oligos) are described in Figure 2.

Please replace the paragraph on page 12, lines 30-35 with the following paragraph:

a) **VI Cassette**

The variable region of the light chain of the human engineered antibody, hP67 (~~engineered~~ engineered according to International Patent Specification WO91/09967) was PCR cloned with oligos S4503 and S4504. S4503 introduces a 5' Hind III site and S4504 a 3' Spe I site. The PCR product was restricted with Hind III and Spe I and subcloned into pBluescript KS+®.

Please replace the paragraph on page 13, lines 1-6 with the following paragraph:

b) **Vh Cassette**

The variable region of the heavy chain of the human engineered antibody, hP67 (engineered according to International Patent Specification WO91/0997) was PCR cloned with oligos S4501 and S4502. S4501 introduces a 5' Hind III site and S4502 a 3' Spe I site. The PCR product was restricted with Hind III and Spe I and subcloned into pBluescript KS+®.

Please replace the paragraph on page 13, lines 8-11 with the following paragraph:

c) **CD8* Spacer Cassette**

The CD8* spacer cassette was PCR assembled using overlapping oligos: S4881, S4882, S4883, S4884, S4885 and S4886. The PCR product was restricted with Spe I and Not I and subcloned into pBluescript KS+®.

Please replace the paragraph on page 13, lines 13-18 with the following paragraph:

d) **CD4 TM / CD4 Cassette**

The CD4 transmembrane and intracellular components were PCR cloned from human Leukocyte cDNA (Clontech) with oligos S4499 and S4500. S4499 introduces a 5' Not I site and S4500 introduces a 3' _EcoR I and Sac I site. The PCR product was restricted with Not I and Sac I and subcloned into a pBluescript KS+®.

Please replace the paragraph on page 13, lines 26-27 with the following paragraph:

The PCR product was restricted with Not I and EcoR I and substituted for the CD4 TM/CD4 cassette in pBluescript KS+®.

Please replace the paragraph on page 13, lines 29-31 with the following paragraph:

All of the above cassettes were sequenced (Applied Biosystems, Taq DyeDeoxy Terminator Cycle Sequencing, Part Number 901497) in pBluescript KS+® prior to cloning into expression vectors.